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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/667,236 | 09/17/2003 | Susan Gregory | BIOL0019US | 6787 |
| 27180 | 7590 | 10/11/2005 | EXAMINER | |
| ISIS PHARMACEUTICALS INC 1896 RUTHERFORD RD. CARLSBAD, CA 92008 | | | HAMA, JOANNE | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1632 | |

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|---------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/667,236 | Applicant(s) GREGORY, SUSAN | |
| | Examiner Joanne Hama, Ph.D. | Art Unit 1632 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-25 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

[Handwritten signature]

This Application was filed September 17, 2003 and claims no additional priority.

Claims 1-25 are pending.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-12, drawn to a mouse model for bone metabolism, comprising exposing a mouse to a compound selected from the group of parathyroid hormone (PTH), an analogue of PTH, and a fragment of PTH for a time sufficient whereby serum calcium concentration and RANKL mRNA expression are increased in the model, and methods for screening for a potentially therapeutic agent which affects bone metabolism, and for assessing the activity of potentially therapeutic agents useful for the treatment and prevention of osteoporosis, comprising administering the agent to the mouse model and assessing the mouse for an alteration in a bone metabolism related marker affected by the agent, classified in class 800, subclass 18.
- II. Claims 13-25, drawn to a method for testing a mouse model for bone metabolism disease comprising administering an antisense oligonucleotide to RANK or RANKL to the mouse, administering to the mouse a compound selected from the group consisting of parathyroid hormone (PTH), an analogue of PTH, and a fragment of PTH, and assessing the effect of the antisense oligonucleotide on the mouse compared to a

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control mouse not treated with the antisense oligonucleotide, classified in class 800, subclass 3.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-II are patentably distinct. Invention I is drawn to a mouse model of osteoporosis, wherein making the model entails administering parathyroid hormone (PTH), an analogue of PTH, or a fragment of PTH, whereby serum calcium concentration and RANKL mRNA expression are increased in the model. Invention I is also drawn to methods of using the mouse model to screen and assess potential agent that treat or prevent osteoporosis. Invention II is distinct from Invention I because Invention II depends on the use of antisense oligonucleotides. The search for Inventions I and II is burdensome because the searches are not coextensive.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, recognized divergent subject matter, and that the search for one Invention is not required for the other, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention:

Claims 1 and 13 are comprised of multiple species of compounds to which a mouse model of bone metabolism is exposed:

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- a. parathyroid hormone (PTH) and a fragment of PTH,
- b. an analog of PTH.

One compound must be selected.

Claim 22 is comprised of multiple species of antisense oligonucleotides which are used on the mouse model of a bone metabolism disease:

- 1. SEQ ID NO. 180,
- 2. SEQ ID NO. 185,
- 3. SEQ ID NO. 356,
- 4. SEQ ID NO. 357.

One SEQ ID NO. must be selected.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-17, 19-25 are generic for the compound to which the mouse model of bone metabolism is exposed and claims 13-25 are generic for the antisense oligonucleotide to RANK or RANKL.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

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Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

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272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file

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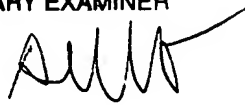
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folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Anne M. Wehbe', with a long horizontal stroke extending to the right.